Design of an Implantable Insulin Pump using Ferromagnetic Soft Material

Undergraduate Honors Thesis

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by

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Abstract

Diabetes mellitus more often called diabetes is a chronic condition that raises levels of glucose in the blood because the body cannot produce any or enough of the hormone insulin or use insulin effectively. When left untreated, high levels of glucose in the blood continue and cause damage to various body organs, leading to the development of disabling and life-threatening health complications. Unfortunately, no cure has been found for diabetes at this moment. However, these serious complications can be prevented or delayed with appropriate management. Current methods of insulin delivery require multiple daily injections or continuous subcutaneous insulin infusions, causing a delay in insulin absorption and possibly creating an infection. These disadvantages can be solved with an implanted device. However, only implantable insulin devices introduced required a large battery inside the body. The purpose of this research is to design an implantable insulin pump that is small and uses untethered control through the ferromagnetic soft material actuator and magnetic field generator for control. This device consists of a balloon, ferromagnetic soft material, two check valves, and an insulin reservoir. Externally, the battery-powered magnetic field will be created to deform ferromagnetic soft material and squeeze the balloon to inject insulin. The ferromagnetic soft material is fabricated and magnetized for controlled deformation, by controlling balloon deformation with an accurate external magnetic field, precise insulin injection is possible without any of the discomfort that current insulin delivery devices give. In this research, the major objectives are to design of battery-less implantable insulin pump using a ferromagnetic soft material, create a profile between the magnetic field and fluid flow, construction of system and test for its accuracy and precision. Finally, test data will be compared with the FEM simulation date. This will show the feasibility of this implantable insulin pump design

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Chapter 1: Introduction

1.1 Background

Diabetes mellitus more often called diabetes is a chronic condition that raises levels of glucose in the blood because the body cannot produce any or enough of the hormone insulin or use insulin effectively [1]. Insulin is an essential hormone produced in the pancreas which allows your body to turn glucose into energy called glycogen. Glucose is the primary energy source in the body for muscle and organs. It is the smallest of sugar that is broken down from carbohydrates after consumption for better transportation in the body. Glycogen is another form of sugar that is better suited for storage in the liver and muscles easily. These two forms of carbohydrate are constantly shifting in the body to maintain the energy required. During meal time, the body contains more glucose than it requires so insulin is produced to convert it to glycogen and between the meal time glucagon is produced to reverse the process.

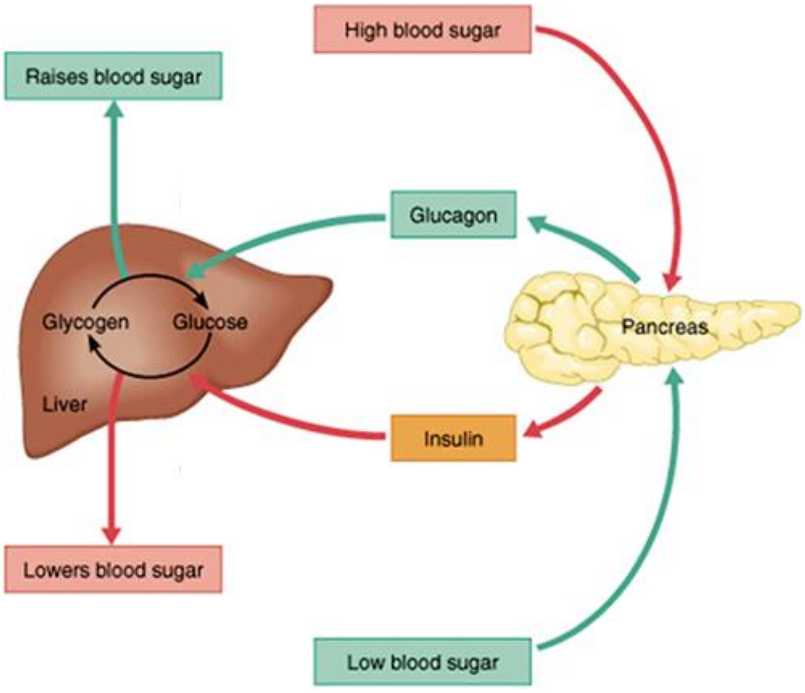

Figure 1. Cycle of Carbohydrate in the Body

For diabetes patients, this process is not properly working in their body and stays at high glucose levels more than the body can stand. When this is left untreated and high levels of glucose in the blood continues over the long term, it can cause damage to various body organs, leading to the development of disabling and life-threatening health complications like heart disease, stroke, kidney damage, nerve damage, blindness, and amputations of the legs and feet [2]. CDC, Centers for Disease Control and Prevention has reported diabetes as the seventh leading cause of deaths with 80,058 deaths in the United States in 2016 [3].

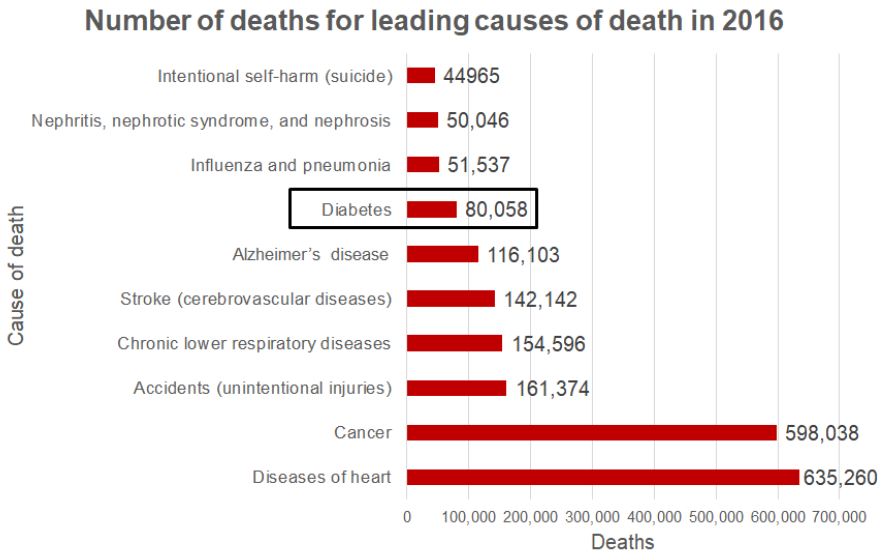

Figure 2. Number of Death for Leading Cause of Death in 2016

Additionally, the population of diabetes has been increasing in the US. CDC also reported that it was estimated that more than 30 million US population had it in 2015 which matches the diabetes population prediction made in 2009 as shown in figure 3.

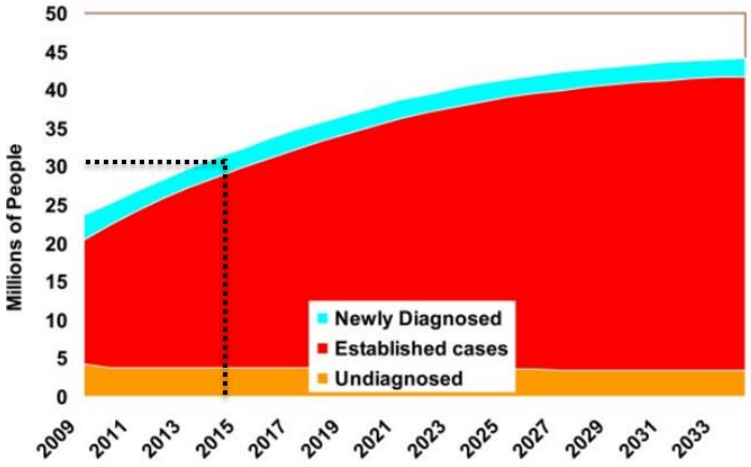

Figure 3. Projected Diabetes Population from 2009

Diabetes is also a significant problem to the society in the form of higher medical costs, decreased productivity, early mortality, and low quality of life. The estimated economic burden due to diabetes in the United States in 2012 was $327 billion [4].

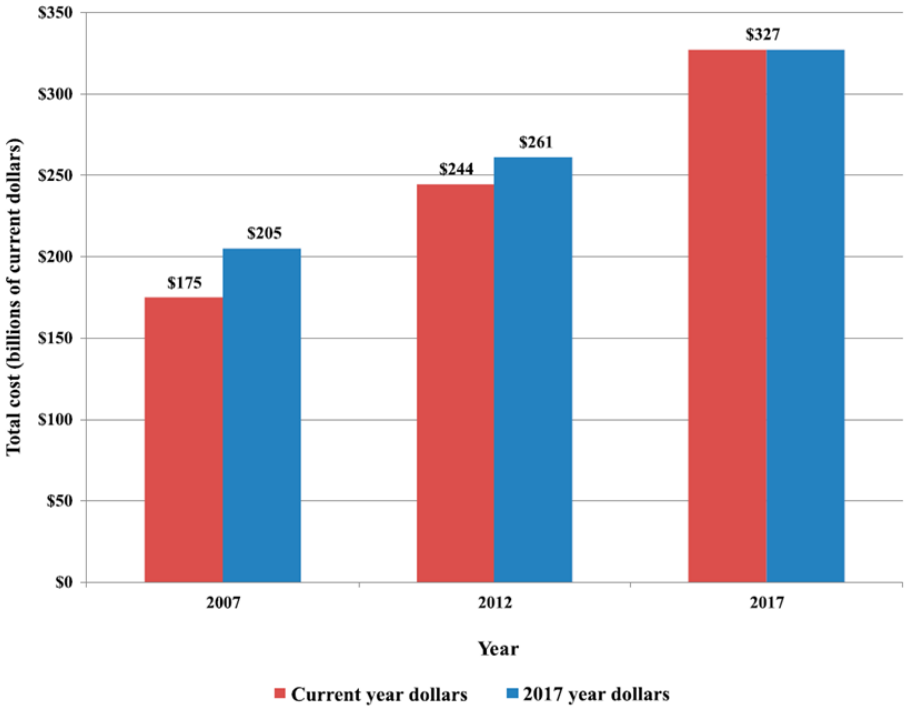

Figure 4. The Cost of Diabetes

Not all diabetes is the same for every patient. When looked deeper into diabetes, there are mainly two types of diabetes, type 1 and type 2 diabetes. Type 1 diabetes is caused by the body's immune system attacking the insulin-producing beta cells in the pancreas, resulting in the inability to create insulin [1]. Type 2 diabetes, which is around 90% of all cases of diabetes, is due to the body's insufficient production of insulin and resistance of the insulin produced from the body [1]. A most important part of managing both types of diabetes patients is to maintain optimal levels of glucose in the blood which is between 70~150mgdl [5]. To accomplish this, a constant monitor of levels of glucose and accurate injection of the insulin is required. To deliver insulin into the bloodstream, the injection system is required. If too much insulin is injected and the glucose level goes below the optimal level, which creates hypoglycemia. Multiple studies are being conducted to create a cure for diabetes using gen modifications and other methods. Unfortunately, at this moment, there is no cure for diabetes. However, these serious complications can be prevented or delayed with appropriate management. Among different management, the most important one is the injection of insulin to the body to maintain the optimal level of glucose in the blood.

1.2 Current Insulin Injection Method

Currently, there is various insulin injection method available to patients in the market. The most common methods are using a syringe, insulin pen, and insulin pump. These methods use subcutaneous injection. The main advantage of the syringe and insulin pen is its affordability compared to other methods. However, cons weights over the pros as patients are responsible for accurate injection. It requires a series of training and preparation, an injection can be painful when done inaccurately, rotation of injection site, subcutaneous injection creates time lag for

insulin to travel to the bloodstream. Lastly, patients need to use active glucose measurement is required to find the exact insulin amount to inject.

Another method is using an insulin pump. It solved a lot of complications that the syringe and insulin pen had by eliminating training, preparation, pain from the injection, and other complications. The reason this was possible is through continuous glucose monitor (CGM) which can constantly track glucose level in the blood and send the data to the insulin pump to calculate the accurate amount of insulin and automatically inject through injection port as shown in figure 5. This allows diabetic patients to forget about the injection and have a more flexible diet. This helps patients to feel less like the patient and have a more active life which helps to mitigate diabetes. For these reasons, an insulin pump is currently the closest method to mimic the pancreas in the market.

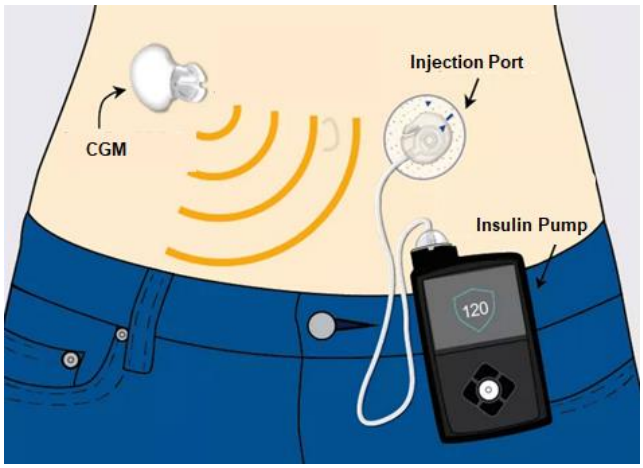

Figure 5. Schematics of Insulin Pump

However, even insulin pumps still cannot solve the problem of the time lag of insulin absorption, risk of skin infection at the injection port, and liphohypertrophy, a condition from injecting insulin at one site for a long period of time causing lump filled with extra fat to rise. Additionally, having a large pumping device on the waist with a constant open injection port

makes patients be less active. The insulin pump is also a very expensive device costing more than $6,000.

Figure 6. Liphohypertrophy

1.3 Implantable Insulin Pump

To solve the time lag of insulin absorption and the risk of a skin infection, a more direct injection method called intraperitoneal (IP) infusion is introduced. IP infusion injects a substance into the peritoneum, a body cavity to be absorbed via the capillaries. By using IP infusion, insulin can be delivered directly to the liver which follows the path of naturally produced insulin from the pancreas. Many case studies show faster absorption speed compared to subcutaneous injection and better control of glucose level in blood.

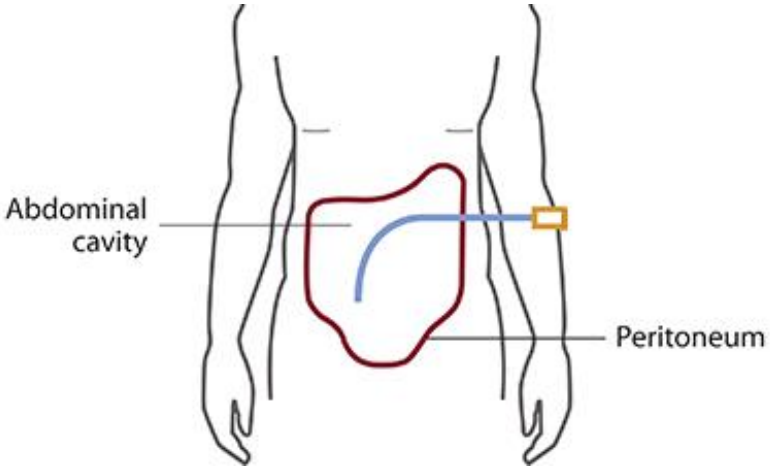

Figure 7. Intraperitoneal (IP) Infusion

Unfortunately, as IP infusion method requires deeper penetration, constant external injection method like insulin pump becomes too risky with possible penetration of diseases. Therefore, different means of insulin pump had to introduce for internal injection. And this is why an implantable insulin pump (IIP) is presented. IIP also is known as an artificial pancreas, is an insulin pumping device implanted to the body with an insulin reservoir that can be externally refilled. There have been several IIP types of research and development promotion but only one product has made it to the market. Dr. Christopher Saudek from John Hopkin's Diabetes Center implanted the first MiniMed implantable insulin pump in 1986.

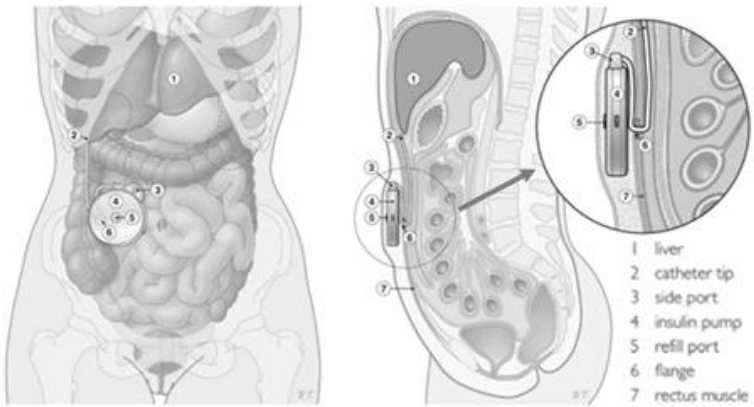

Figure 8. Schematics of MiniMed Implantable Insulin Pump

Figure 9. Photo of MiniMed Implantable Insulin Pump

However, the device did not last long. In 2007 Medtronic purchased MiniMed and stopped the research trials in the United States [6]. The reasoning behind the discontinuation is from too many complications of the system. The main complication was from the battery inside the implanted device. At the time, the battery was not efficient enough for long time use and easily failed even before the predicted life of the pump. Additionally, having a battery itself is dangerous due to its enormous amounts of energy in a small volume and is surrounded by several hazardous materials [5]. Implanting such an energy source in the inner body, a special space filled with electrical, chemical, mechanical, and marine-salted reactions, can unstabilize the battery quickly [6]. As a result, many patients went through additional surgery for replacement. This is why even though many case studies show MiniMed IIP performance better in maintaining the glucose level in the blood and multiple patients' testimony of improved lifestyle, Medtronic discontinued the device.

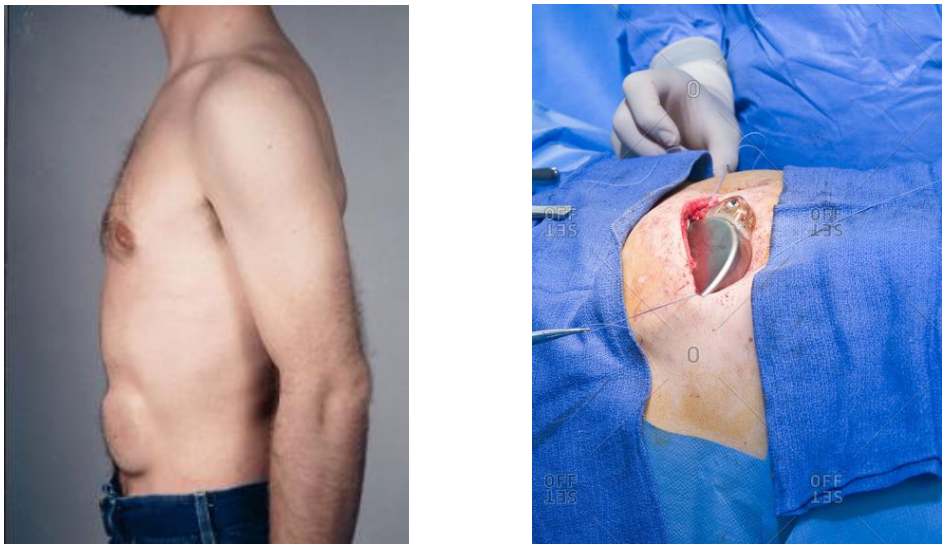

Figure 10. Surgical Process of MiniMed Implantable Insulin Pump

Even though the MiniMed IIP was not successful, the improved result it showed in maintaining the optimal glucose level in blood is undeniable. Therefore, it is necessary to develop an implantable insulin pump that can overcome the complication that MiniMed IIP had and this can be achieved by removing the battery from the implanting pump system.

1.4 Significance of Research

Removing the battery from the pump system means that the pump needs to operate wirelessly. When looking at the forces in nature, the magnetic force is the one that can achieve this and materials that react to the magnetic force are called ferromagnetic materials that exhibit strong magnetism in the same direction of the field, when a magnetic field is applied to it. However, these materials are solids that make it heavy and difficult to implement with other systems. This is where the idea of ferromagnetic soft material can be used. By mixing soft materials like polymer and ferromagnetic materials in powder form with directionality given, it is

possible to achieve flexible material that can be controlled with a magnetic field. With this, a simple but effective mechanical pump can be designed.

As seen in figure 11, the pump system consists of a balloon, actuator made of ferromagnetic soft material, two check valves, and an insulin reservoir. Two one-way valves are placed on each side of the balloon to block any reverse flow, the Actuator is placed on top of the balloon, and the reservoir is connected to the balloon. Externally, a battery-powered magnetic field generator will be placed on top of where the pump system is located. This way when the magnetic field is generated, it will deform the actuator which will squeeze the balloon to inject insulin. Next, when the magnetic field is turned off, the actuator will come back to the original shape and the balloon will inflate again with insulin from the reservoir.

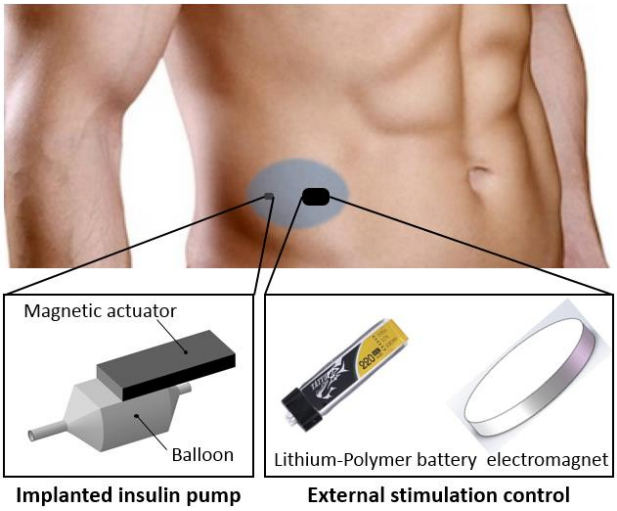

Figure 11: Schematics of New Implantable Insulin Pump

In this research, the major objectives are to design of battery-less implantable insulin pump using a ferromagnetic soft material, create a profile between the magnetic field and fluid flow, construction of system and test for its accuracy and precision. Finally, test data will be compared with the FEM simulation data. This will show the feasibility of this implantable insulin pump design.

Chapter 2: Methodology

2.1 Fabrication of Ferromagnetic Soft Material

As previously mentioned, ferromagnetic soft material is a mixture of soft material like polymer with ferromagnetic materials in powder form. In this study, polydimethylsiloxane (PDMS) was mixed with neodymium iron boron alloy powder (NdFeB). One interesting feature of polymer is the ability to obtain different material properties by varying the ratio of mixture between the NdFeB powder, PDMS base, and curing agent. For this study, 20% NdFeB with a 20:1 ratio of base to an agent for PDMS was used. To create this ferromagnetic soft material, first, a calculation is required to obtain the weight of each material. Next, each material is poured into a container after weighing. Then, for the thorough mixing process, the container is placed in the centrifuge machine. This mixture is then poured on to mold as demonstrated in figure 12. Two different mold shape is needed for this step, one is for the actual actuator with a dimension of 14mm x 10mm x 2mm and another for the tensile test as seen in figure 13 and 14. Once placed on the mold PDMS takes about 20 hours to cure and harden. This process can be accelerated by placing the mixture in the oven with 80.

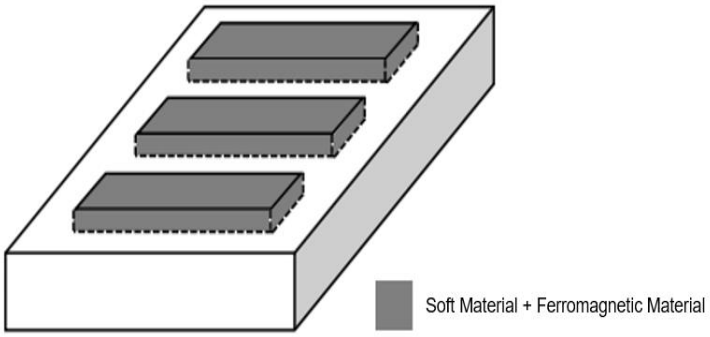

Figure 12: Molding, Fabrication method of Ferromagnetic Soft Material Mold

Figure 13: Ferromagnetic Soft Material for Actuator

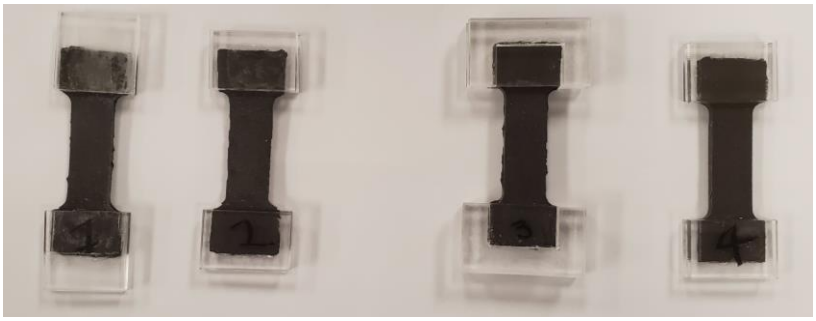

Figure 14: Ferromagnetic Soft Material for Tensile Test

2.2 Tensile Test

Once the material is cured, the tensile test is conducted to find the material properties. For material model, uniaxial extension - Incompressible Neo-Hookean solid, a hyperelastic material model was chosen to represent nonlinear stress-strain behavior. Next, from the test machine, the stress-strain data is collected. This data is imported to the MATLAB where coefficient, is calculated using curve fitting application with the neo-Hookean material equation. After conducting three tests, averaging the value was obtained. Using the equation below, shear modulus, and elastic modulus is calculated for this ferromagnetic soft material.

$$\text{neo} - \text{Hookean Material equation, } \sigma = 2C_1(\lambda - \frac{1}{\lambda^2})$$

$$Shear\ Modulus, G = 2 * C_1$$

$$Elastic\ Modulus, E = 2G(1 + v)$$

$$\text{For incompressible material, v} = 0.5$$

$$E = 3G$$

2.3 Magnetization

With ferromagnetic soft material molded for the actuator, magnetization is conducted to give magnetic directionality. Initially, when the ferromagnetic soft material is cured, iron particles start at the lowest energy state where the magnetic domain is random. However, the magnetic domain is not fixed in place. Under the strong external magnetic field, the domain walls will move by the process of the spins of the electrons in atoms near the wall in one domain turning under the influence of the external field to face in the same direction as the electrons in the other domain, thus reorienting the domains as seen in figure 15. Additionally, the domains will remain aligned when the external field is removed, creating a magnetic field of their own extending into the space around the material, thus creating a "permanent" magnet. The domains do not go back to their original minimum energy configuration when the field is removed because the domain walls tend to become pinned to the defects in the crystal lattice, maintaining their parallel orientation.

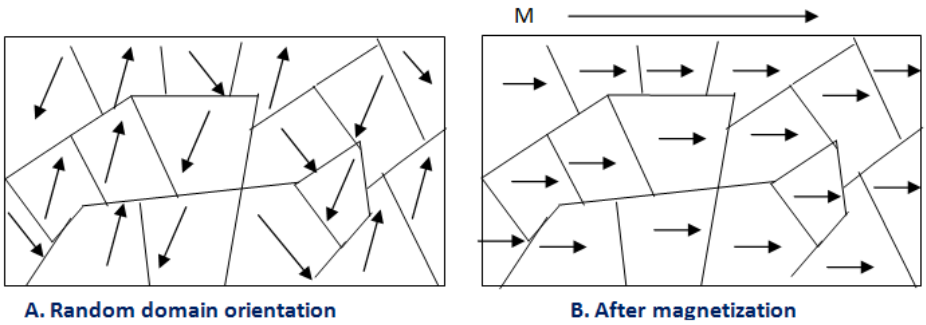

Figure 15. Magnetic domain change under external magnetic field

2.4 Magnetic Field & Deflection

Once the magnetization on the actuator is completed, a test on deflection under a magnetic field can be conducted. First, the magnetic field is measured at each increment of voltage supply from 0V to 15V as shown in figure 16. Then, the actuator is placed on the center of the magnetic field generator to measure the deflection. To verify, the simulation was conducted with fixed one end and load at the other end representing the magnetic force on a beam.

Figure 16: Magnetic Field Measurement

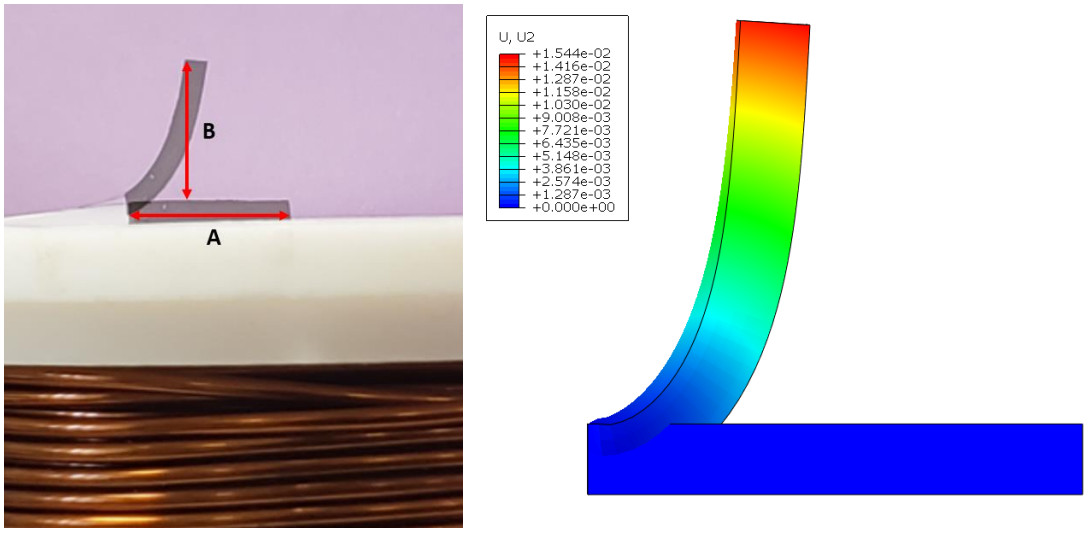

Figure 17: Actuator Deflection Measurement and Simulation

Voltage Supply (V)	*Magnetic Field (mT)*	*Deflection (mm)*
0	0	0.00
1	0.7	1.06
3	4	4.55
5	7.8	7.32
7	11.3	8.94
9	15.1	10.13
11	19.3	11.01
13	23.6	11.70
15	26	12.04

Table 1: Magnetic Field and Deflection Measurement

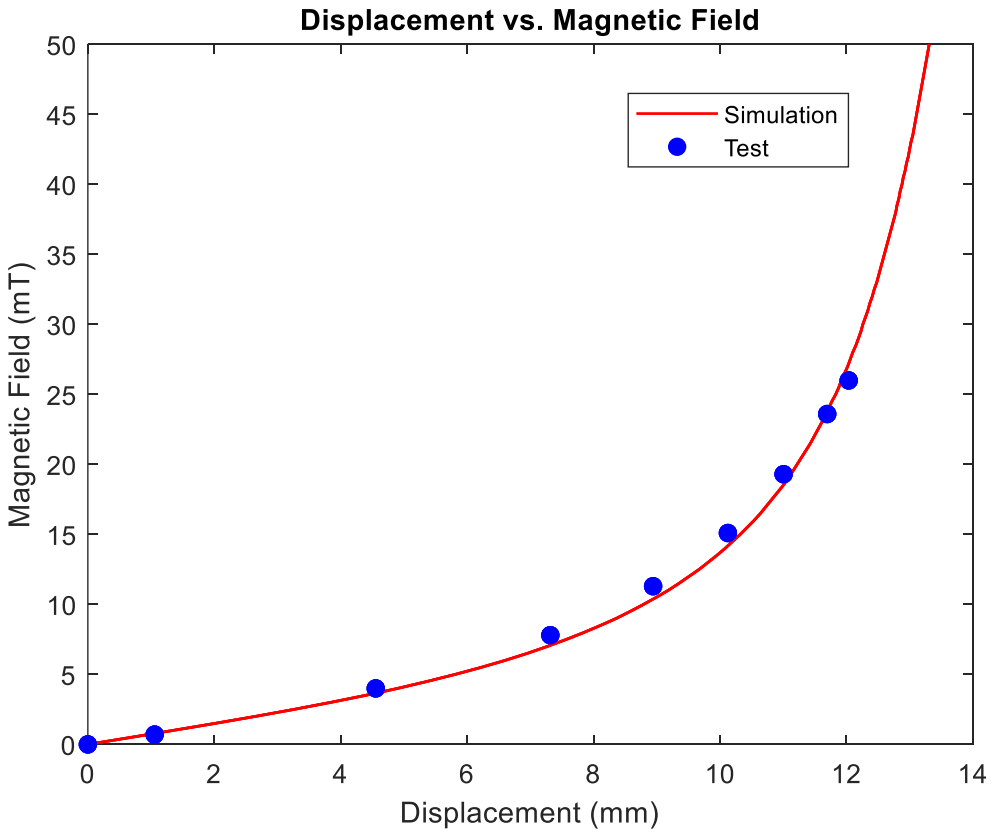

Figure 18: Displacement vs. Magnetic Field Plot

2.5 Force & Volume Change

The next test setup is for the fluid flow which mimics the implanted environment. Setup is constructed as shown in Figures 19 and 20. The pump system is unattached with a magnetic field generator by a 2mm layer of acrylic just like the implanted pump system would be separated by the skin. From this test setup, the volume of fluid pushed through the pump is measured by measuring the length of the tube traveled by the fluid and multiplied the area for volume.

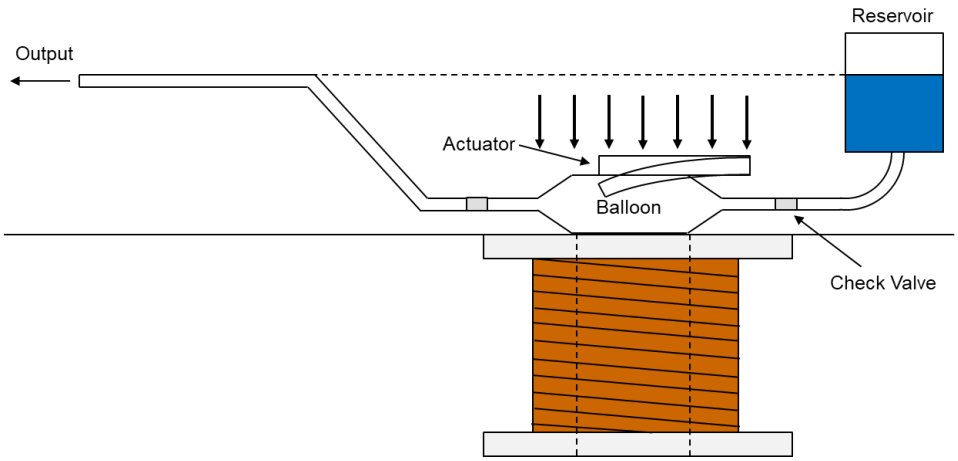

Figure 19. Schematics of Fluid Flow Test Setup

Figure 20. Photo of Actual Test Setup

In the simulation, two material, actuator and balloon are introduced. The actuator used material property obtained from the tensile test and balloon use material property of thermoplastic polyurethane elastomer which had Young's Modulus, E = 13.1MPa with Poisson's ratio, v = 0.5 for incompressible solid. Then, fix boundary condition was given to the left end of the actuator and bottom of the balloon as seen in figure 21. Constant pressure was given inside the balloon to represent the fluid pressure. Lastly, displacement instead of force was given to the right end of the actuator for better convergence. Equivalent force to displacement is found by the reaction force. Once the simulation was completed, the volume of flow is obtained by converting the deformed balloon in the STL file and measure the volume with MATLAB *volume* command and subtracting it from the original volume.

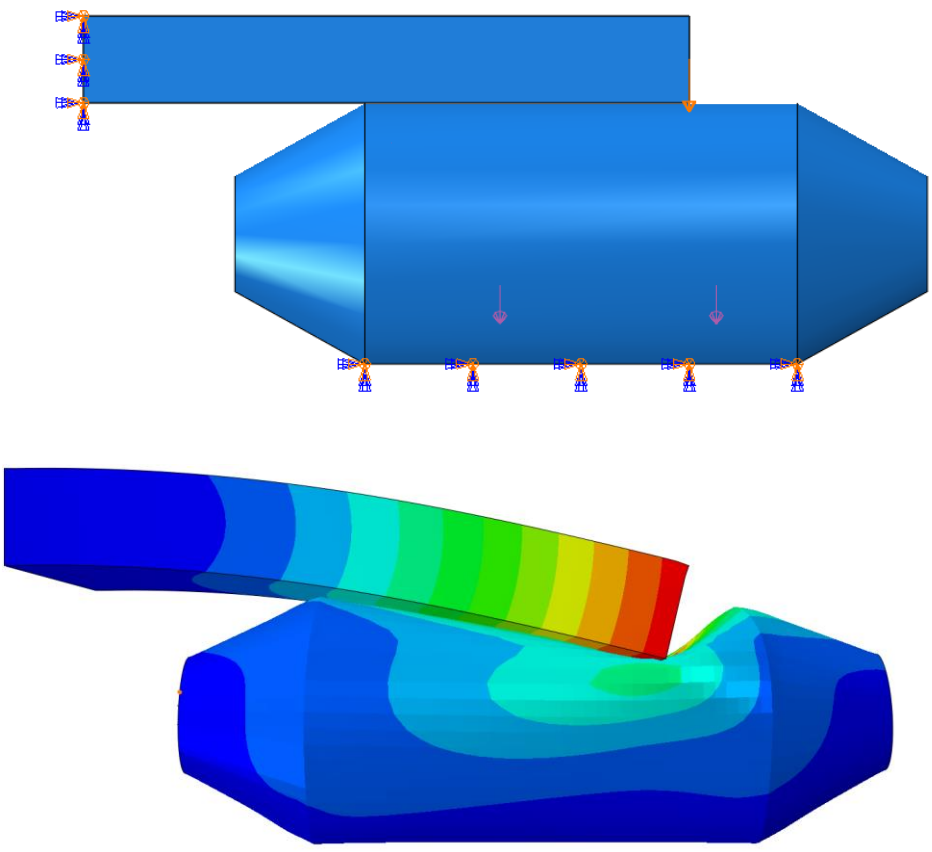

Figure 21: Image of Fluid Flow Boundary Condition and Simulation Result

Figure 22 shows a plot of simulation data for volume change with an increase of force exerted on the actuator. By utilizing the magnetic field – force relationship obtained in the previous step, data is converted to volume change with an increase of the magnetic field. Finally, an exponential trend line representing the characteristic of this pump design is obtained using curve fitting application in MATLAB and shown in figure 23. Lastly, two sets of test data are compared with simulation data in figure 24. It is shown that simulation and test match in the small magnetic field, but difference increases as the magnitude of the magnetic field increases. This is due to errors in the balloon from the test setup where the balloon does not always start at a fully inflated state.

$$y = a * exp(b * x) - a$$

$$a = 0.7504$$

$$b = 0.1243$$

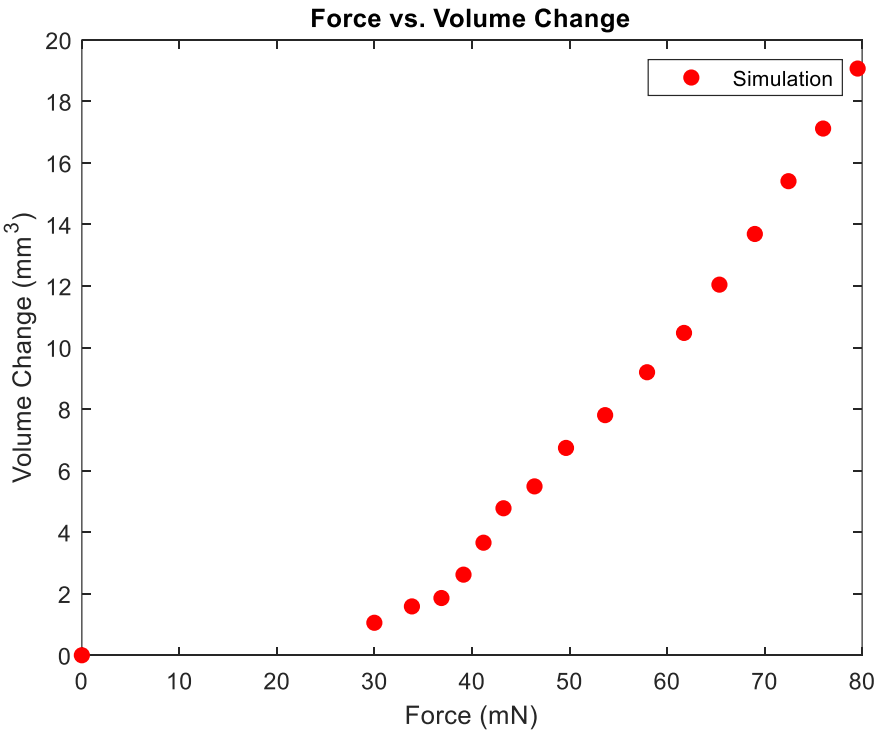

Figure 22: Force vs. Volume Change Plot

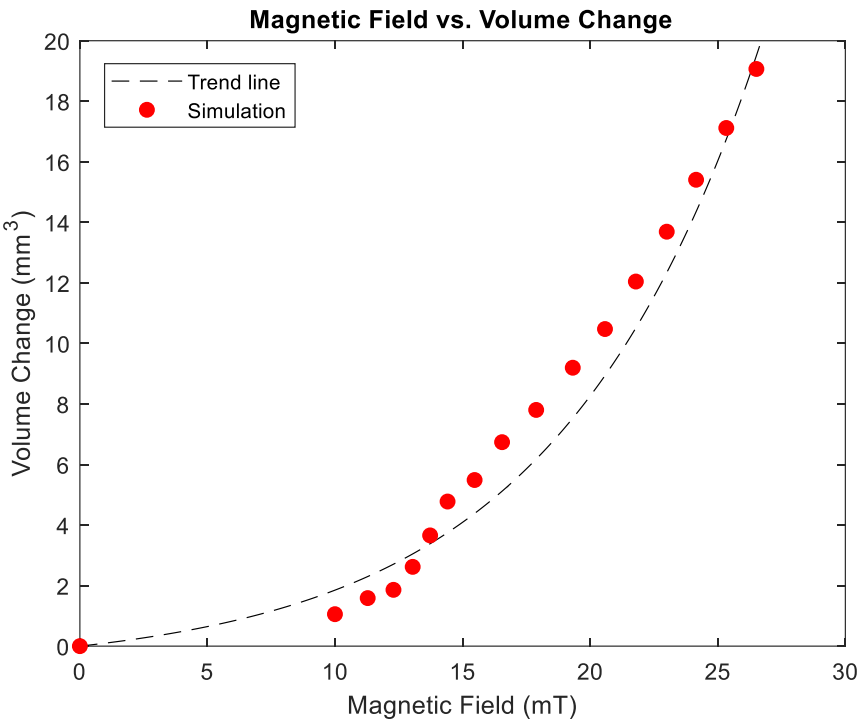

Figure 23: Magnetic Field vs. Volume Change Plot with Trend Line

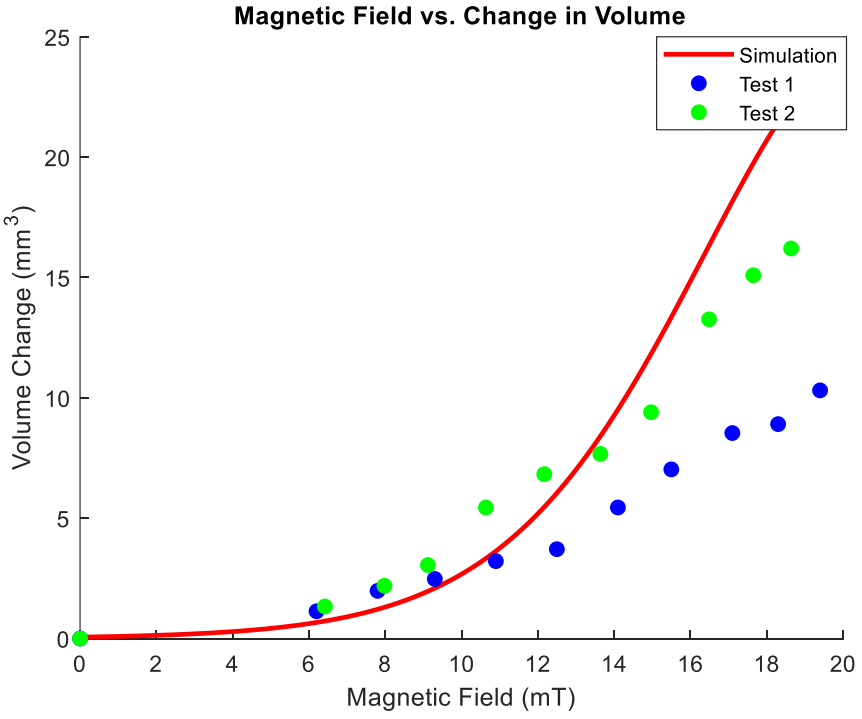

Figure 24: Magnetic Field vs. Volume Change with Test data

Chapter 3: Conclusion & Future Work

3.1 Conclusion

To conclude, a battery-less implantable insulin pump using ferromagnetic soft material that can be affordable and help diabetes patients glucose level in blood is designed and tested along with FEM simulation and was able to obtain a profile between the magnetic field and fluid flow. Even though this profile is unique for this design, the ability to create a different profile that matches the need shows room for improvement. This research has successfully demonstrated the feasibility of an implantable insulin pump without any battery or electronics. Lastly, a prototype was designed and fabricated as shown in Figures 25 and 26.

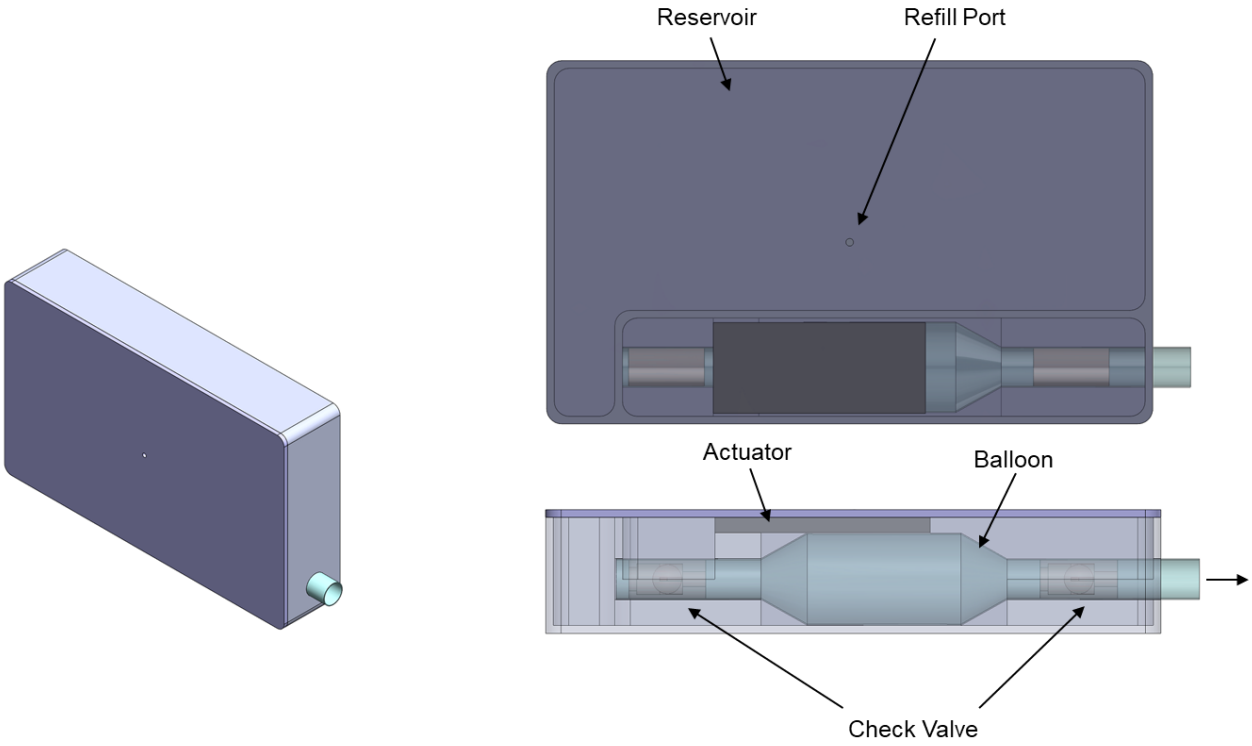

Figure 25: Prototype Design

Figure 26: Prototype Fabrication

3.2 Future Work

For future work, to complete this implantable insulin pump system, the design of the portable battery-powered uniform magnetic field generator is needed. Additionally, animal testing through coordination with the medical company and further investigation on ways to minimize the design size using smaller components will help this implantable insulin pump closer to the becoming real product.

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